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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,142	04/13/2004	Jean-Marc Guillaume	FRAV2003/0009 US NP	4542

5487 7590 05/15/2007

ROSS J. OEHLER
SANOFI-AVENTIS U.S. LLC
1041 ROUTE 202-206
MAIL CODE: D303A
BRIDGEWATER, NJ 08807

EXAMINER	
BARNHART, LORA ELIZABETH	

ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
05/15/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPatent.E-Filing@sanofi-aventis.com
andrea.ryan@sanofi-aventis.com

Office Action Summary	Application No.	Applicant(s)	
	10/823,142	GUILLAUME ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *5,6 and 9-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/30/04*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *4/30/07*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

A requirement for restriction was mailed in this case on 9/27/06. However, due to a typographical error, claims 70-75 were inadvertently omitted from this requirement. The Groups set forth below should substitute for the Groups in the 9/27/06 restriction requirement. Specifically, claims 70-75 have been placed into Groups XX and XXI.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-8, drawn to a method for obtaining mastocytes comprising culturing bone marrow stem cells, classified in class 435, subclass 377.

II. Claim 9, drawn to porcine mastocytes that may be obtained from the method of Group I, classified in class 435, subclass 325.

III. Claims 10-16 and 22-47, drawn to porcine mastocytes with particular properties, classified in class 435, subclass 325.

IV. Claim 17, drawn to a porcine mastocyte line, classified in class 435, subclass 325.

V. Claim 18, drawn to another porcine mastocyte line, classified in class 435, subclass 325.

VI. Claim 19, drawn to another porcine mastocyte line, classified in class 435, subclass 325.

VII. Claim 20, drawn to another porcine mastocyte line, classified in class 435, subclass 325.

VIII. Claim 21, drawn to another porcine mastocyte line, classified in class 435, subclass 325.

IX. Claim 48, drawn to a method for culturing the mastocytes of Group III to produce heparin-type molecules, classified in class 435, subclass 325.

X. Claim 49, drawn to a method for producing heparin-type molecules by culturing porcine mastocytes, classified in class 435, subclass 325.

XI. Claim 50, drawn to another method for producing heparin-type molecules by culturing porcine mastocytes, classified in class 435, subclass 325.

XII. Claim 51, drawn to another method for producing heparin-type molecules by culturing porcine mastocytes, classified in class 435, subclass 325.

XIII. Claims 52 and 53, drawn to a protein of porcine origin of the c-kit type, classified in class 514, subclass 2+.

XIV. Claims 54-58, drawn to a nucleic acid encoding a protein of porcine origin of the c-kit type, classified in class 536, subclass 22.1+.

XV. Claim 59, drawn to a cell expressing a protein of porcine origin of the c-kit type, classified in class 435, subclasses 325+, 410+, or 243+.

XVI. Claims 60 and 61, drawn to a protein of porcine origin exhibiting 3-O-sulfatase activity, classified in class 514, subclass 2+.

XVII. Claims 62-66, drawn to a nucleic acid encoding a protein of porcine origin exhibiting 3-O-sulfatase activity, classified in class 536, subclass 22.1+.

XVIII. Claim 67, drawn to a cell expressing a protein of porcine origin exhibiting 3-O-sulfatase activity, classified in class 435, subclasses 325+, 410+, or 243+.

XIX. Claims 68 and 69, drawn to a protein of porcine origin exhibiting 6-O-sulfatase activity, classified in class 514, subclass 2+.

XX. Claims 70-74, drawn to a nucleic acid encoding a protein of porcine origin exhibiting 6-O-sulfatase activity, classified in class 536, subclass 22.1+.

XXI. Claim 75, drawn to a cell expressing a protein of porcine origin exhibiting 6-O-sulfatase activity, classified in class 435, subclasses 325+, 410+, or 243+.

The reasons these inventions are distinct from each other were set forth in the 9/27/06 restriction requirement and still apply to this Office action.

Applicant's election without traverse of Group I, claims 1-8, in the reply filed on 2/23/07 is acknowledged. A telephone call to Agent Wang on 4/30/07 confirmed that the election in the 2/23/07 reply (*i.e.*, Group I, claims 1-8, without traverse) still applies to the prosecution in light of the new groupings.

The 2/23/07 reply expressly indicates that the election is "without traverse" (Reply, page 1, paragraph 1), but the examiner notes that applicant has requested rejoinder of Groups II and III to elected Group I at such time as Group I becomes allowable (Reply, page 1, paragraph 2), and Agent Wang repeated this request on the phone. The rejoinder provisions under *In re Ochiai*, however, provide only for the rejoinder of allowable method claims when product claims are elected, but not for the

rejoinder of products to elected process claims. Examining the products in Groups II and III would require a search field that is distinct from that required to search the elected method for the reasons set forth in the restriction requirement, and applicant has not particularly traversed the restriction requirement between Group I and Groups II and III; as such, the request for rejoinder is denied at this time.

It is noted that applicant replied to the 9/27/06 requirement on 2/23/07; however, the reply was incomplete because applicant elected Group I (claims 1-8) but neglected to elect a species of "source of stem cells" as directed on page 8 of the 9/27/06 requirement. In a telephone call on 4/30/07, Agent Wang elected species (b), "human fetal bone marrow," with traverse. Affirmation of this election must be made by applicant in replying to this Office action.

In the 2/23/07 reply, applicant urges that Groups XX and XXI are substantial repeats of Groups XIV and XV (Reply, page 1, paragraph 1); however, this miscommunication was due to a typographical error, and it is believed that the replacement Groups set forth above clarify the restriction requirement.

Claims 9-75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/23/07 and was confirmed in a 4/30/07 telephone conversation with applicant's representative. Claims 5 and 6 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim.

Applicant timely traversed the restriction (election) requirement in a telephone conversation on 4/30/07.

Examination on the merits will now commence on claims 1-4, 7, and 8 ONLY.

Specification

The abstract of the disclosure is objected to because it is not at least 50 words, it does not describe the invention sufficiently, it recites language that can be implied, and it recites legal language. Correction is required in the form of a replacement abstract. See MPEP § 608.01(b).

Applicant is reminded of the proper content, language and format for an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and **should include that which is new in the art to which the invention pertains.** If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

The abstract should be in **narrative form** and generally limited to a single paragraph on a separate sheet within the range of **50 to 150 words**. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. **The form and legal phraseology often used in patent claims**, such as "means" and "said," **should be avoided**. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. **It should avoid using phrases which can be implied**, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The disclosure is objected to because of the following **FOUR** informalities, each of which requires appropriate correction in response to this Office action.

1. The spacing of the lines of the specification is such as to make reading difficult. New application papers with lines 1½ or double spaced on good quality paper are required. See MPEP § 608.01(b) (2) (ii).

2. Numerous words are misspelled in the specification, for example "chimiokines" for "chemokines" at line 22 of page 1 of the as-filed specification; "Quiaquick" for "QIAQuick" and "Quiagen" for "QIAgen" at line 7 of page 24.

3. The as-filed specification lacks the section headings required by 37 C.F.R. 1.77(b). For example, the brief description of the drawings appears to commence at page 14 of the as-filed specification, but there is no section heading to this effect.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.

(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

4. The use of the trademarks "MEM" (page 15, line 30), "CYTOFIX/CYTOPERM" (page 16, line 29, *e.g.*), "PERMAWASH" (page 16, line 30, *e.g.*), "PERM/WASH" (page 17, line 27, *e.g.*), "SPHERISORB" (page 19, line 21), "NUCLEOFECTION" (page 21, line 33), "ZEOCIN" (page 23, line 18), "QUIAQUICK [*sic*]" (page 24, line 7), "FIRST STRAND SYNTHESIS" (page 24, line 49, *e.g.*), "TRIZOL" (page 24, line 46, *e.g.*), "ZERO BLUNT" (page 25, line 10, *e.g.*), "GATEWAY" (page 25, line 46, *e.g.*), "ADVANTAGE" (page 27, line 17, *e.g.*), and "GENETICIN" (page 29, line 34, *e.g.*), to name a few has been noted in this application. These and all trademarks should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. The specification

should be carefully reviewed for any trademarks that are not properly formatted as above. No new matter may be introduced.

Information Disclosure Statement

The listing or recitation of references in the specification (as, for example, at page 4, lines 27-28, of the as-filed specification) is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

The information disclosure statement (IDS) submitted on 4/30/04 was filed before the mailing date of the first Office action on the merits. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner is considering the information disclosure statement. It is noted for the record that no English translation was provided for WO03/035853 and WO/035886.

Claim Objections

Claims 1-4 are objected to because of the following informalities: They recite the abbreviations "SCF," "IL," and "G-CSF" without particularly defining the same. Appropriate correction is requested.

The words "bone marrow" are hyphenated in claims 1, 7, and 8, as are the words "human fetal" in claim 7, which is inconsistent with standard written English. Correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 7, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to "a method for obtaining mastocytes," but the claim does not contain any step in which mastocytes are produced. The steps within the method are not commensurate in scope with the preamble of the claim. There is no step, for example, in which the bone marrow stem cells are cultured until mastocytes are obtained; therefore, the steps do not necessarily result in the production of mastocytes. Clarification is required.

Because claims 2-4, 7, and 8 depend from indefinite claim 1 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Besmer et al. (1999, U.S. Patent 5,935,565; reference A) taken in view of Sugimoto et al. (2001, *Mie Medical Journal* 51: 59-65; reference U) and Kikuchi et al. (2002, U.S. Patent 6,383,480; reference B).

Besmer teaches a method comprising culturing murine bone marrow (BM), which inherently comprises stem cells, in IMDM culture medium (column 45, lines 20-32) comprising 10 ng/mL KL (*i.e.*, c-*kit* ligand, also called stem cell factor, SCF) along with either 1 ng/mL G-CSF (Figure 25) or a mixture of 50ng/mL IL-6 (interleukin-6) and sufficient IL-3 to promote CFU-C stimulation (column 45, lines 34-54; Figures 25 and 26). Besmer teaches that culturing BM in this manner results in enhanced production of mast cells (*i.e.*, mastocytes; column 3, lines 1-4); specifically, that culturing murine BM in IL-3-containing media for at least 4 weeks yields mastocytes (column 35, line 63, through column 36, line 7).

Besmer does not teach a medium comprising IL-4. Besmer does not exemplify a medium comprising both IL-6 and G-CSF. Besmer does not exemplify culturing human bone marrow stem cells.

Sugimoto teaches that culturing murine BM (page 60, column 1, under "Cell preparation") in culture medium comprising 10ng/mL steel factor (*i.e.*, c-*kit* ligand, also called stem cell factor, SCF) along with 10ng/mL IL-3 and 10ng/mL IL-4 promoted the formation of mastocytes -containing colonies (page 60, column 1, "Growth factors"; Table 2, lines 8 and 11; page 62, column 1, paragraph 2, *inter alia*).

Kikuchi teaches that IL-3, IL-4, IL-6, and G-CSF show a synergistic effect with SCF on both murine and human hematopoietic stem cells (column 1, line 43, through column 2, line 2).

A person of ordinary skill in the art would have had a reasonable expectation of success in adding IL-4 to the culture medium of Besmer to yield mastocytes because Sugimoto teaches that IL-4 acts synergistically with SCF and IL-3 to produce mastocyte-containing colonies. Similarly, the skilled artisan would have had a further reasonable expectation of success in combining the SCF/G-CSF medium of Besmer with the SCF/IL-3/IL-6 medium of Besmer because Besmer teaches that both promote stem cell amplification and mast cell formation. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted). See M.P.E.P. § 2144.06. The skilled artisan would have been motivated to include IL-4 and G-CSF in the culture medium for the expected benefit that the yield of mastocytes would be increased.

A person of ordinary skill in the art would have had a reasonable expectation of success in substituting human bone marrow for the murine bone marrow of Besmer because Kikuchi teaches that the effects of SCF, IL-3, IL-4, IL-6, and G-CSF are synergistic on both types. The skilled artisan would have been motivated to make this substitution in order to produce human mastocytes.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to culture BM (either human or murine) in a culture medium comprising the claimed amounts of SCF, IL-3, IL-4, IL-6, and G-CSF because Besmer, Sugimoto, and Kikuchi teach that these growth factors and cytokines in these amounts promote mast cell production from bone marrow.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lora E Barnhart